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(54) Title of the Invention: DRUG FOR ORAL CAVITY

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Specification

[Translator's note: Additions and deletions based on an attached page of amendments filed by the applicant Showa Denko and dated December 27, 1985, are incorporated in the translated text and indicated by the "track changes" function (deleted original text is struck out and new text underlined).]

1. Title of the Invention

Drug for Oral Cavity

2. Claims

A drug for the oral cavity characterized as containing an L-ascorbic acid-2-phosphate or a salt thereof as an active ingredient.

3. Detailed Description of the Invention

(Industrial Field of Application)

The present invention relates to a drug for the oral cavity that is effective for the prevention and treatment of periodontosis, cleaning of the oral cavity, elimination of halitosis, and freshening of the mouth, and contains a stable derivative of ascorbic acid.

(Prior Art and Related Problems)

Ascorbic acid strengthens capillary vessels by aiding the production of mucopolysaccharides contained in the connective tissue, and strengthens the oral cavity structure by contributing to the hydration of proline and stimulating the production of collagens. It further manifests an antimicrobial action on bacteria in the oral cavity that are a cause of plaque, which contributes tooth decay and gum disease.

Nevertheless, since ascorbic acid is a strongly reductive substance and is easily oxidized, losing its effect and producing marked discoloration, it has been extremely difficult to adapt as a drug for the oral cavity.

In light of these circumstances, the present inventors, as the result of intensive and varied research aimed at obtaining a drug for the oral cavity that has sufficient activity of ascorbic acid but is also extremely stable; found that L-ascorbic acid-2-phosphates and their salts are suitable as drugs for the oral cavity.

(Constitution of the Invention)

Specifically, the present invention provides a drug for the oral cavity containing as its effective ingredient an L-ascorbic acid-2-phosphate or a salt thereof, such as a sodium, potassium, calcium, or magnesium salt.

L-ascorbic acid-2-phosphates and their salts are both safe and extremely stable, readily dissolve in water, and exhibit excellent effect in the prevention and treatment of periodontosis, since the effects of ascorbic acid are sufficiently manifested when the compound is used in the living body.

The oral composition of the present invention may be used in various forms of death difference such as toothpaste, powder or liquid, or can be formulated in other forms such as chewing gum, paste, gargle, or troche.

The amounts blended vary according to the formulation and therefore cannot be uniformly prescribed, but generally is appropriate to contain this ingredient in the amount of 0.01 to 10% (wt.%). While there is no strict limitation with respect to the amount used in effective ingredient conversion, normally, 0.1 to 5 g per day is appropriate, and can be increased or decreased as necessary.

Next, representative working examples of the present invention are described, but of course

the present invention is not restricted to these examples alone.

Working Example 1

A toothpaste was prepared by normal methods in accordance with the following recipe:

Ingredients	Wt %
calcium diphosphate dihydrate	45.0
sodium carboxymethylcellulose	0.5
carrageenan	0.5
glycerin	10.0
sorbitol	10.0
fragrance	1.0
preservative	0.1
sodium saccharin	0.1
sodium lauryl sulfate	2.0
sodium chloride	2.0
ascorbic acid magnesium phosphate	1.0
water	remainder

Working Example 2

A gargle was prepared by normal methods in accordance with the following recipe:

Ingredients	Wt %
95% ethyl alcohol	35.5%
glycerin	14.0%
fragrance	1.0%
ascorbic acid magnesium phosphate	1.0%
water	remainder

Working Example 3

A troche was prepared by normal methods in accordance with the following recipe:

Ingredients	Wt %
white sugar	85.0%
magnesium stearate	1.0%
high propyl cellulose	8.0%
menthol	trace
ascorbic acid magnesium phosphate	3.0%

Working Example 4

A chewing gum was prepared by normal methods in accordance with the following recipe:

Ingredients	Wt %
gum base	65.0%
mannit	20.0%
fragrance	2.0%
70% sorbit	3.0%
ascorbic acid magnesium phosphate	1.0%

(Effect of the Invention)

(1) Safety Test

The safety of an oral composition containing L-ascorbic acid-2-phosphate was confirmed using SD rats five weeks of age. The oral composition used was prepared in accordance with the method of Working Example 1 described above.

30 rats having an average weight of 131.2 g were divided into two groups. The oral composition of Working Example 1 was administered to one group, while the same oral composition of Working Example 1 described above without L-ascorbic acid-2-phosphate was administered to the other group orally twice a day for 10 days. After 11 days the rats were sacrificed, tissue was removed from the gums and mucous membrane and saliva glands from the oral cavity of the rats among and tissue fragments were observed by microscope using normal methods. As a result, it was confirmed that no pathological changes occurred in the tissue in comparison with the 15 animals in the contrast group, to which L-ascorbic acid-2-phosphate was not administered.

(2) Stability Test

Next, the stability of various oral compositions containing L-ascorbic acid-2-phosphate was studied, and the results are shown.

The oral compositions used were prepared in accordance with the recipe of Working Example 1 described above. The oral compositions were each store at 50°C for 10 days, 20 days and 30 days, and discoloration was evaluated in accordance with the following standards.

A: no discoloration, B: slight discoloration, X: marked discoloration

The results are shown in Table 1.

(Table 1) Change in the color of oral compositions containing L-ascorbic acid-2-phosphate at 50°C

	10 days	20 days	30 days
L-ascorbic acid-2 magnesium phosphate 10%	B	B	B
5%	A	A	B
3%	A	A	A
1%	A	A	A
ascorbic acid 10%	X	X	X
5%	B	X	X
3%	B	X	X
1%	B	B	X
Not added (contrast group)	A	A	A

As is shown in Table 1, the oral composition to which L-ascorbic acid-2-phosphate was added was highly stable and extremely resistant to discoloration even when ascorbic acid was added.

In addition, precisely 50 mg ascorbic acid magnesium phosphate was dissolved in 100 ml water, and the aqueous solution obtain was allowed to stand for 30 days, and changes in the L-ascorbic acid-2-phosphate were followed by high-speed liquid chromatography, but even after 30 days the amount of ascorbic acid magnesium phosphate showed little change, and it was confirmed that ascorbic acid magnesium phosphate is extremely stable in an aqueous solution.

The high-speed liquid chromatography performed was measured on the following conditions using the JASCO UV-DEC 100 manufactured by JASCO.

Column: Shodex OH pak Q-801

Elution liquid: (Na_2So_4 0.05 mol/H_3PO_4 0.05 mol)/L
Flow rate: 0.7 ml/min Detection method: UV 257 nm
Pressure: 8 kg/cm^2

(3) Efficacy Test

20 patients (males aged 25 to 45 years) having various periodontal diseases such periodontosis and marginal gingivitis were divided into two groups of 10 patients each, with patients with the same degree of symptoms evenly distributed between the two groups. One of the groups was treated for 60 days twice a day, in the morning and evening, with the oral composition containing ascorbic acid magnesium phosphate in accordance with the recipe of Working Example 1 described above. The other group used as a control was traded with an oral composition (2 g) having the same recipe as in Working Example 1 described above but not containing ascorbic acid magnesium phosphate.

As an indicator of efficacy, in the event of improvement of one item among the pathological fluctuation and relaxation, bleeding, pathological gingival [illegible] formation, gingival discoloration, retraction of the gums, severe halitosis, one point was awarded, and the number of points was tabulated for improvement of multiple items.

On the other hand, in the case of aggravation of symptoms among the aforesaid items, minus one point was awarded, and in the case of no change, zero points were awarded, and the final number of points for each patient was tabulated.

The results are shown in Table 2. The value shown by the total points divided by the number of patients.

(Table 2)

	10 days	20 days	30 days	40 days	50 days	60 days
Oral composition containing L-ascorbic acid-2-phosphate	+0.4	+0.9	+0.6	+1.2	+1.5	+1.7
Contrast group: Oral composition not containing L-ascorbic acid-2-phosphate	-0.5	-0.3	-0.3	-0.4	-0.3	-0.2

It is clear from the results in Table 2 that the oral composition containing the ascorbic acid phosphate was extremely efficacious against periodontal diseases.

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